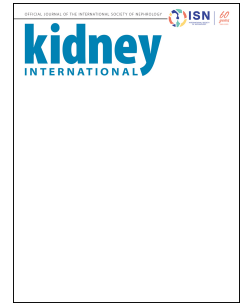




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Breakthrough Omicron COVID-19 infections in patients receiving REGEN-Cov antibody combination

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COVID-19 vaccines are efficient to prevent severe COVID-19 infections. Immunocompromised patients are at increased risk of both severe COVID-19 and poor immunologic response to anti-SARS-CoV-2 vaccines.

Pre-exposure prophylaxis using anti-spike neutralizing monoclonal antibodies to prevent COVID-19 infection has been proposed as an alternative in patients with no immunologic response after three doses of COVID-19 vaccines^{1,2}. We herein provide the first report, to our knowledge, of breakthrough COVID-19 infections in immunocompromised patients treated preventively with REGEN-Cov (Casirivimab + Imdevimab).

Between September 24th and December 23rd, 2021, 80 patients who had received at least 3 doses of COVID-19 vaccine and had a negative anti-SARS-CoV-2 spike protein antibody response received at least one injection of 600 mg of Casirivimab and Imdevimab for pre-exposure prophylaxis in our center (**Figure 1**). Causes of poor immunologic response to vaccination were kidney transplantation (n=57, 71%), treatment with rituximab (n=9, 11%), end-stage kidney disease (n=7, 9%), and other (n=7, 9%). All patients were asked to report COVID-19 infection.

Among this cohort, we received twelve reports of COVID-19 infection between December 25th, 2021, and January 18th, 2022 (**Figure 1**). SARS-CoV-2 infection was diagnosed using an antigenic test in one case and by PCR test in the remaining 11 cases. The Omicron variant (lack of L452R mutation) was detected in 8 cases, while screening for Omicron was unavailable in the remaining 3 PCR-proven cases. Two patients were hospitalized due to severe symptoms but did not require a transfer in the Intensive Care Unit. These breakthrough COVID-19 infections due to the Omicron variant are consistent with *in-vitro* evidence of a complete escape of SARS-CoV-2 variant Omicron to Casirivimab and Imdevimab^{3,4}.

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Figure 1. Occurrence of COVID-19 breakthrough infections are associated with the occurrence of the Omicron variant in Ile-de-France, France. Green dashed line: cumulative number of REGEN-Cov administrations. Red line: cumulative number of COVID-19 infections among patients treated with REGEN-Cov in our cohort. Black curve: COVID-19 incidence rate in Ile de France, France, per 100.000 inhabitants. Blue area: proportion of COVID-19 cases with suspected Delta variant (presence of L452R mutation) in Ile-de-France, France. Red area: proportion of COVID-19 cases with suspected Omicron variant (lack of L452R mutation) in Ile-de-France, France. Data for Ile de France was obtained from Santé Publique France (<https://geodes.santepubliquefrance.fr>) on Jan 22nd, 2022.

